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EXAMINER	
LONG, SCOTT	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
09/30/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/763,049	ROBINSON ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-8,11-23,25-27,30-39,42,43 and 52-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-8, 11-23, 25-27, 30-39, 42-43, 52-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Claim amendments, filed on 22 July 2008.

Claim Status

Claims 1-3, 13-119, 23, 32-35, 37, 39, 52-53 have are amended. Claims 4-5, 9-10, 24, 28-29, 36, 40-41, and 44-51 are canceled. Claims 1-3, 6-8, 11-23, 25-27, 30-35, 37-39, 42-43, 52-56 are under current examination.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 31 October 2007 consisting of 3 sheet(s) are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims benefit from as a CON of 08/187,879 filed on 01/27/1994 (US-PAT 6,841,381), which is a CIP of 08/009,833 filed on 01/27/1993 (US-PAT 5,643,578), which is a CIP of 07/855,562 filed 03/23/1992 (ABN). The instant application has been granted the benefit date, 23 March 1992, from the application 07/855,562.

Applicant has argued (Remarks, pages 8-9) that the "retroviral promoter" limitation as recited in the instant claims is entitled to the benefit of priority from application 07/855,562. The examiner accepts this argument.

Therefore, the examiner modifies the benefit as follows: The parent, US-PAT 5,643,578, does not have benefit of (1) SIV antigen, (2) rotavirus antigen, (3) microsphere encapsulation of DNA, (4) methods of immunization comprising combinations of influenza antigens. Therefore these limitations will be given the benefit of US-PAT 6,841,381, filed on 27 January 1994.

RESPONSE TO ARGUMENTS

Response to Arguments - Claim Rejections 35 USC § 112, 2nd parag.

Claim 17 rejected under 35 U.S.C. 112, second paragraph, is withdrawn in response to the applicant's claim amendments and/or arguments

Applicant's arguments (Remarks, page 9) and claim amendments regarding rejection of claim 17 rejected under 35 USC 112, 2nd paragraph, filed 22 July 2008 have been fully considered and they are persuasive.

The applicant has amended claim 17 to resolve the antecedent basis issue.

Therefore, the examiner hereby withdraws the rejection of claim 17 rejected under 35 U.S.C. 112, second paragraph.

Response to Arguments - Claim Rejections 35 USC § 112, 1st parag. (new matter)

Claims 1-4, 6-8, 11-23, 25-27, 30-35, 37-39, 42-43, 52-56 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter) is withdrawn in response to the applicant's arguments and/or claim amendments.

Applicant's arguments (Remarks, pages 9-11) and claim amendments, filed 22 July 2008) regarding rejection of claims 1-4, 6-8, 11-23, 25-27, 30-35, 37-39, 42-43, 52-56 under 35 USC 112, 1st paragraph, have been fully considered and they are persuasive.

The applicant has submitted that the specification provides implicit support for the concept of DNA vaccination using a "mixture of plasmid vectors" and suggests that page 14, lines 28-30 and page 24, lines 25-26 indicate this support. Specification page 14, lines 28-30 states, “DNA units were diluted in saline at a concentration of 100 ug per 0.2 ml for inoculation.” Page 14, lines 31-21 bridging page 15, lines 1-2 state, "To test the ability of the inoculated DNA to protect against a lethal influenza virus challenge, groups of three week old chicks were inoculated with pP1/H7, p188, or pRCAS DNA." As skilled artisan would interpret this to mean that each chick was inoculate with a single plasmid and not a mixture of plasmids. However, the specification does provide support for “a mixture of DNA transcription units” (page 10, lines 16-17), but does not explicitly support multiple different plasmids. The examiner can accept that it is an obvious variation to provide the mixture of DNA transcription units on different plasmids rather than on the same plasmid. Therefore, the examiner will withdraw the new matter rejection on this basis, in part, because the applicant has argued that a plasmid in a pharmaceutically acceptable carrier is encompassed by the recited claim language (specifically, see Spec., page 10, middle paragraph).

The applicant has amended some claims to recite “a plurality of the same plasmid vectors.” The examiner is uncertain how this is different from “a composition consisting essentially of the plasmid vector" since administration of a plasmid vector is typically administered in micrograms of plasmid, meaning that there are millions of copies of the same plasmid. The examiner would interpret this as "a plurality of the same plasmid vectors." The examiner does not understand the reason for including

this language, but accepts that it is not critical to the invention and does not distinguish the claims from a typical DNA vaccine.

The applicant has argued that the specification provides implicit support for the transitional support for "consisting essentially of." The examiner accepts this statement, since there is support in the specification for plasmids in saline.

Therefore, the examiner hereby withdraws the rejection of claims 1-4, 6-8, 11-23, 25-27, 30-35, 37-39, 42-43, 52-56 under 35 USC 112, 1st paragraph (new matter).

Response to Arguments - Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 1-3, 6-8, 11-23, 25-27, 30-35, 37-39, 42-43, 52-56 under 35 U.S.C. 103(a) as being unpatentable over Felgner et al. (WO90/11092) in view of Huylebroeck et al. (Gene. June 1988. 66(2): 163-81) and further in view of Townsend et al. (Cell. November 1984; 39(1):13-25) and further in view of Atkinson et al. (US-

4,861,864, issued 29 Aug 1989) and further in view of Andrianov et al. (US-5,529,777, issued 25 June 1996) are maintained.

Applicant's arguments (Remarks, pages 11-16) and claim amendments, filed 22 July 2008) regarding rejection of claims 1-3, 6-8, 11-23, 25-27, 30-35, 37-39, 42-43, 52-56 under 35 USC 103 have been fully considered but they are unpersuasive.

The applicant has amended the instant claims to include a limitation directed to "whereby a protective immune response comprising a humoral immune response, a cell-mediated immune response, or both is elicited against the antigen, to protect the vertebrate against a subsequence infection by an influenza virus or a rotavirus." The applicant argues "none of the references, individually or combined, suggest that a DNA vaccine could be used successfully to protect a subject from a subsequence viral infection" (Remarks, page 12, lines 7-8).

Contrary to the applicant's argument, Felgner et al. teach, "Normal vaccination schemes will always produce a humoral immune response….The humoral system protects a vaccinated individual from subsequent challenge from a pathogen" (page 3, lines 33-36). Absent evidence to the contrary, the method of DNA vaccination against influenza virus or rotavirus as suggested by Felgner et al. in view of Huylebroeck et al. and further in view of Townsend et al. and further in view of Atkinson et al. and further in view of Andrianov et al. would provide protection of a vaccinated individual from subsequent challenge from a pathogen. Therefore, the examiner finds the applicant's argument unpersuasive.

Accordingly, the examiner hereby maintains the rejection of claims 1-4, 6-8, 11-23, 25-27, 30-35, 37-39, 42-43, 52-56 under 35 U.S.C. 103(a) as being unpatentable over Felgner et al. in view of Huylebroeck et al. and further in view of Townsend et al. and further in view of Atkinson et al. and further in view of Andrianov et al.

The examiner reiterates the rejection of from the previous Action, below:

Claims 1-3, 6-8, 11-23, 25-27, 30-35, 37-39, 42-43, 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Felgner et al. (WO90/11092) in view of Huylebroeck et al. (Gene. June 1988. 66(2): 163-81) and further in view of Townsend et al. (Cell. November 1984; 39(1):13-25) and further in view of Atkinson et al. (US-4,861,864, issued 29 Aug 1989) and further in view of Andrianov et al. (US-5,529,777, issued 25 June 1996).

Claims 1 and 16-17 are directed to methods of immunizing a vertebrate using a composition consisting essentially of a set of plasmid vectors in a physiologically acceptable medium, the plasmid vectors comprising DNA encoding an influenza virus antigen or a rotavirus antigen operatively linked to a DNA promoter, which elicits a humoral and/or cell-mediated immune response against a desired antigen. Claim 4 is directed to the limitation that the method is capable of eliciting a protective immune response. Claims 7 and 25-26 are directed to the further limitation that the virus is an influenza virus and the antigen is hemagglutinin. Claims 8 and 27 are directed to the further limitation that the virus is a rotavirus. Claims 30-31 are directed to the limitations of delivery to a “human mammal.” Claim 32 is directed to using a gene gun to administer the compositions of the invention. Claims 15 and 23 are directed to

administration of microsphere encapsulated plasmid vectors in a physiologically acceptable medium. The instant specification does not specifically define the scope of "microsphere encapsulated plasmid vectors." The specification's sole embodiment of microsphere encapsulated plasmid vectors is as alginate microspheres. Furthermore, the specification does not exclude liposome microspheres from being considered pharmaceutically acceptable.

Felgner et al. teach plasmid vectors comprising "therapeutic polynucleotides… [which] code for immunity-conferring polypeptides, which act as endogenous immunogens to provoke a humoral or cellular response, or both" (page 17, lines 31-34). Felgner et al. suggest that tumor-specific antigens and viral protein antigens are appropriate for use in their invention (for example, page 4). Felgner et al. also teach intradermal, intramuscular administration (page 11, lines 33-37) of naked polynucleotides in pharmaceutically acceptable carriers (page 8, line 24) to vaccinate a human (page 8, line 34). Furthermore, Felgner et al. teach "polynucleotides may be...delivered into muscle or skin using a vaccine gun" (page 36, lines 15-18). Felgner et al. also teach liposomal microsphere formulations of plasmid DNA and administration to the lung; the examiner believes this satisfies the limitations directed to pharmaceutically acceptable microsphere encapsulated plasmid vectors, in light of the teachings of the specification, described above.

Felgner et al. do not teach specific antigens for influenza or rotavirus. Felgner et al. also do not specifically teach administration of set of plasmids encoding antigens, although they do teach co-transfection of two different plasmids to the cells.

Huylebroeck et al. teach plasmid DNA mediated gene transfer of two different influenza A antigens, including H1 hemagglutinin (abstract). Huylebroeck et al. teach cotransfection of plasmids and co-expression of hemagglutinin A and influenza matrix protein M_1 in animal cells.

Townsend et al. teach plasmids comprising hemagglutinin antigens. Townsend et al. also teach "isolated full-length influenza gene clones is now routine" (page 13, col.2). Furthermore, Townsend et al. teach, "there are implications for vaccine design…a vaccine that presents nucleoprotein in an appropriate form that could stimulate crossreacrtive CTL memory might be crossprotective between pandemic influenza A viruses" (page 22, col.2).

Atkinson et al. teach a plasmid comprising cDNA of a rotavirus antigen for expression of VP7 (col. 4, lines 39-42). Atkinson et al. teach that an object of their invention is to provide a neutralizing antigen to rotavirus which is readily disseminated throughout the body with the concomitant greater exposure to the immune system (col.2, lines 34-37).

Huylebroeck et al. and Townsend et al. and Atkinson et al. do not specifically teach DNA vaccines. These references also do not teach immunization using sets of plasmids encoding the antigens.

Andrianov et al. teach "polymeric hydrogels are used to encapsulate antigen to form vaccines….microparticles are formed ….preferred polymers are alginate" (abstract) and "enhanced immunogenicity of microspheres formed of 95% alginate" (col., lines) and methods of oral and mucosal delivery. Andrianov et al. teach "the

polymer is used to deliver nucleic acid which encodes antigen to cells where the nucleic acid is expressed" (col.12, lines 39-42).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to immunize a vertebrate against an influenza virus or rotavirus by administering a composition consisting essentially of a set of plasmid vectors comprising DNA encoding either influenza virus antigens or rotavirus antigens. Furthermore, it would have been obvious to use microencapsulation of plasmid DNA or gene gun to administer the DNA vaccines. In addition, it would have been obvious to use sets of plasmids to administer plasmids comprising antigens.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (plasmids comprising influenza or rotavirus antigens, methods of DNA vaccination, and gene gun administration) are taught by Felgner et al. or Huylebroeck et al. or Townsend et al. or Atkinson et al. and further they are used as vaccines or are shown to be involved in inducing Cytotoxic T Lymphocyte responses. It would be therefore predictably obvious to use a combination of these elements in a DNA vaccine. The methods of combining the elements with "sets of plasmids" are predictable; and therefore they are likewise obvious. Co-administration of plasmids has been performed in the art and is merely a variation of administration. Also, Andrianov et

al. suggests alginate microspheres for use in vaccines; therefore, it would be obvious to apply this technology to plasmid DNA vaccine formulations.

Therefore the method as taught by Felgner et al. in view of Huylebroeck et al. and further in view of Townsend et al. and further in view of Atkinson et al. and further in view of Andrianov et al. would have been *prima facie* obvious over the method of the instant application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 8, 11-23, 27, 30-35, 39, 42-43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1-16

of U.S. Patent No. 6,165,993. Although the conflicting claims are not identical, they are not patentably distinct from each other because: The claims of both the instant application and the issued patent are directed to DNA vaccination using plasmids encoding rotavirus epitopes. Furthermore, both contain limitations directed to microsphere-encapsulated plasmids.

Claims 1-3, 8, 11-23, 27, 30-35, 39, 42-43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1-27 of U.S. Patent No. 6,187,319. Although the conflicting claims are not identical, they are not patentably distinct from each other because: The claims of both the instant application and the issued patent are directed to DNA vaccination using plasmids encoding rotavirus epitopes. Furthermore, both contain limitations directed to microsphere-encapsulated plasmids.

Claims 1-3, 6-7, 11-13, 16, 30-34, 37-38, 42-43, and 52-56 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 5,643,578 (as first rejected in the Action, filed 9/25/2006 and maintained 5/4/2007). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of USPat-5,643,578, are a species of the more broadly claimed genus encompassed by the instant application.

Claims 1 and 16 of the instant application are broadly drawn to methods of immunizing that elicit an immune response against a desired antigen. Claim 1 of the issued patent, USPat-5,643,578, teaches a method of immunization that protects a vertebrate from a disease caused by an infectious agent. A method of immunization that protects a vertebrate from a disease caused by an infectious agent would have elicited an immune response. The referenced patent states the "term 'immunizing' refers herein to the production of an immune response in a vertebrate which protects (partially or totally) from the manifestations of infection (i.e., disease) caused by an infectious agent." (column 2, lines 48-51). The instant application also contains limitations directed to eliciting a protective immune response against an infectious agent, which is nearly identical to claim 1 of the referenced patent.

Claim 2, 3, 18 and 34 of the instant application are drawn to a nonretroviral promoter, while the specification of the referenced patent teaches CMV promoter, giving the meaning of a nonretroviral promoter to "promoter region" of claims 1, 8, 9, 14, and 17 of the patent.

Claims 6, 25 and 37 of the instant application are directed to the further limitation of the infectious agent being influenza virus. Claims 14-15 and 17-18 of the referenced patent teach, in varying language, the protection against the infectious agent, influenza.

Claim 7 and 38 of the instant application are directed to a desire antigen that is influenza virus hemagglutinin. Claims 1, 15, and 18 of the referenced patent teach the same limitation.

Claims 11, 30 and 42 of the instant application are directed to the limitation that the subject of immunization is a mammal; claims 12, 31 and 43 further limit this mammal to a human. Claims 4-5 and 12-13 of the referenced patent teach the human mammal.

Claim 13 and 32-33 of the instant application are directed a physiologically acceptable carrier and various routes of administration. Claim 6 of the referenced patent teaches the same limitations.

Claim 14 and 17 of the instant application is directed to administration to the mucosal surface. Claim 7-8 and 17 of the referenced patent teach the same limitation.

Claim 21 of the instant application is directed to nasal mucosal surface. Claim 10 of the referenced patent teach the same limitation.

Claim 52 of the instant application is directed to method of immunizing against influenza. Claims 1, 8, 14 and 17 of the referenced patent teach the same method.

Claim 53 of the instant application is directed to a method of immunizing against influenza by administering two or more transcription units comprising different antigens. Claims 1, 8, 14 and 17 of the referenced patent teach a method of immunizing against influenza by administering a DNA transcription unit comprising hemagglutinin or influenza virus antigens. In light of the specification of the referenced patent, a transcription unit may produce one or more antigens, "a DNA transcription unit which comprises DNA encoding a desired antigen or antigens." (column 1, lines 43-44). Accordingly, the referenced patent teaches the limitations of Claim 53 that more than one antigen of influenza is administered for vaccination.

Claims 54-56 are directed to different antigens, different subtypes of influenza.

Claim 19 of the cited patent is directed to the same subject matter.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SDL/ Scott Long
Patent Examiner, Art Unit 1633